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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,495	03/31/2004	Mariah Connelly	10345.200-US	1569

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NOVOZYMES, INC.
1445 DREW AVE
DAVIS, CA 95616

EXAMINER	
KETTER, JAMES S	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,495	CONNELLY ET AL.	
	Examiner	Art Unit	
	James S. Ketter	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,12,15-17,19,20,26,30,33-35,37,38,44,49,52 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,8,12,15-17,19,20,26,30,33-35,37,38,44,49,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7, 8, 12, 15-17, 19, 20, 26, 30, 33-35 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Hjort et al. (designated as reference 2 on the IDS filed 19 April 2004).

Instant claim 1 is drawn to a method of expressing a heterologous biological substance biological substance, comprising culturing a mutant strain of Aspergillus niger which comprises a first nucleotide sequence encoding said substance and one or more second nucleotide sequence which comprises modified glaA gene and, among others, oah gene, and wherein said mutant strain is deficient in glucoamylase production as well as, among others, oxalic acid hydrolase production, all of which followed by recovery of said substance produced. Claim 7 specifies that said substance is a biopolymer, further specified in claim 8 as, among others, a polypeptide. Claim 12 specifies that said substance is a metabolite. Claim 15 specifies that glucoamylase and, read one way, that, among others, oxalic acid hydrolase production is at least 25% lower than the parent strain, while claim 16 more narrowly specifies complete deficiency in production of both. Claim 17 specifies a modification of a proteolytic activity. Claim 19 specifies that one of the recited genes has modified expression of the respective enzyme. Claim 20 is drawn to a mutant strain of Aspergillus niger which comprises a first nucleotide sequence encoding said substance and one or more second nucleotide sequence which comprises modified glaA gene and, among others, oah gene, and wherein said mutant strain is deficient in glucoamylase production as well

as, among others, oxalic acid hydrolase production. Claim 26 specifies that said substance is a biopolymer, further specified in claim 30 as a metabolite. Claim 33 specifies that glucoamylase and, read one way, that, among others, oxalic acid hydrolase production is at least 25% lower than the parent strain, while claim 34 more narrowly specifies complete deficiency in production of both. Claim 35 specifies a modification of a proteolytic activity. Claim 37 specifies that one of the recited genes has modified expression of the respective enzyme.

Hjort et al. teaches, e.g., at page 1, first paragraph, using a strain deficient in oxaloacetate hydrolase activity for production of polypeptides or metabolites. A polypeptide is a biopolymer. At page 34, second full paragraph, mutation of the oxaloacetate hydrolase gene nucleic acid sequence to produce the recited Aspergillus niger is taught. In the subsequent paragraph, mutation to eliminate expression of glucoamylase gene in the Aspergillus niger strain is taught. Also taught at this paragraph is the reduction or elimination of one or more of a number of enzyme activities: aminopeptidase, amylase, carbohydrase, carboxypeptidase, catalase, cellulase, chitinase, cutinase, cyclodextrin glycosyltransferase, deoxyribonuclease, esterase, alpha-galactosidase, beta-galactosidase, alpha-glucosidase, beta-glucosidase, invertase. laccase, lipase, mannosidase, mutanase, oxidase, a pectinolytic enzyme, peroxidase, phospholipase, phytase, polyphenoloxidase, proteolytic enzyme, ribonuclease, transglutaminase, and xylanase. It is particularly taught that this sequence preferably encodes a proteolytic enzyme.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38, 44, 49, 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hjort et al. (2, cited above) in view of Fowler et al. (designated as reference 6 on the IDS filed 19 April 2004).

Instant claim 38 is drawn to a method of producing a mutant strain of Aspergillus niger which comprises introducing into the parent strain a nucleotide sequence which comprises modified glaA gene and, among others, oah gene, and wherein said mutant strain is identified as deficient in glucoamylase production as well as, among others, oxalic acid hydrolase production. Claim 44 specifies that said substance is a biopolymer, further specified in claim 49 that said substance is a metabolite. Claim 52 specifies that glucoamylase and, read one way, that, among

others, oxalic acid hydrolase production is at least 25% lower than the parent strain, while claim 53 more narrowly specifies complete deficiency in production of both.

Hjort et al. is described above. Hjort et al. differs from the invention of the instant claims in not teaching that the mutation in the glaA (glucoamylase) gene is made by insertion of a mutant version on a nucleotide sequence into the parent strain.

Fowler et al. teaches, e.g., at the paragraph extending from page 539-541, including the figures therein, the disruption of Aspergillus niger glaA gene. It is taught that no detectable levels of either the mRNA or protein were present after disruption.

It would have been obvious to one of ordinary skill in the art to have practiced the method of creating the double mutant strain as taught by Hjort et al., with the mutation of the glaA gene being made particularly by the method taught by Fowler et al. The motivation to use the gene disruption method of Fowler et al. would have come from the teaching in Fowler et al. that complete removal of mRNA and protein activity could be accomplished thusly. This would have been an obvious manner to accomplish the teaching of Hjort et al. to eliminate glucoamylase expression, e.g., at the paragraph bridging pages 34 and 35,

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, 8, 12, 15-17, 19, 20, 26, 30, 33-35, 37, 38, 44, 49, 52 and 53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

nucleotides, e.g., said first nucleotide, encoding nucleic acids or polypeptides, does not reasonably provide enablement for a nucleic acid encoding any other class of molecule, e.g., polyamides, polyamines, polyols, polysaccharides or metabolites in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The following factors have been considered in the rejection:

The nature of the invention. A gene may "encode" an RNA or a polypeptide by way of the RNA (mRNA). It might also be argued that a DNA can encode a copy of itself by virtue of the existence of the replication machinery in the cell. However, other types of molecules are included as being "encoded" by the gene in the instant invention.

The state of the art. It is not apparent that the art taught of a way in which a gene could encode a molecule other than a nucleic acid or polypeptide. Of course, such a molecule could be made catalytically by enzymes encoded by the gene, but the actual information content of DNA to RNA to polypeptide ends with the polypeptide sequence, and any metabolic activity catalyzed by the enzyme is merely that, with the enzyme passing no information content along to its substrates. (By analogy, a mechanical drawing could be understood to encode the design of a cutting tool. However, said cutting tool does not pass information about its design along to the material it might be used to cut [except for the trivial case of a cutting tool being used to physically engrave a copy of said mechanical drawing onto said material; even so, the information is not encoded by the cutting tool]).

The amount of direction or guidance presented in the specification, and the presence or absence of working examples. No guidance or examples toward a way in which a molecule

other than nucleic acid or a polypeptide may be encoded by a gene has been set forth in the instant disclosure.

Conclusion. Were the skilled practitioner to have attempted to practice the invention where the gene in question could "encode" a molecule other than a nucleic acid or a polypeptide, said practitioner first would have turned to the specification for guidance. However, no mention of how to transfer information beyond the encoded enzyme was made. Next, said practitioner would have turned to the prior art for such guidance, but again, the art offered no such teachings. Finally, the skilled practitioner would have been forced to turn to empirical experimentation to accomplish this. However, such would involve a fundamental change to the scheme by which genetic information is encoded, passed along and utilized. A means of copying sequence information form the enzyme (polypeptide) would be required in the cell, and such would clearly be an enormous experimental undertaking, representing undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 33 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each instance, the claim recites "the mutant strain produces at least 25% less glucoamylase and one or more enzymes selected from..." However, it is not clear if the "one or

more enzymes" are produced at least 25% less, or only glucoamylase. As such, the metes and bounds of the instant claims are unclear.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James S. Ketter whose telephone number is 571-272-0770. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781 The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSK
20 July 2006

JAMES KETTER
PRIMARY EXAMINER